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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/080,503	02/22/2002	Robert I. Higuchi	015110.0058.UTL1	8671

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EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 07/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/080,503	HIGUCHI ET AL.	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06/24/2002 (IDS)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/24/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1600, Art Unit 1623.

No claims have been cancelled, no claims have been amended, the disclosure has been amended, no new claims have been added and no preliminary amendments have been filed as of the mailing date of this Office action. An Information Disclosure Statement (IDS) filed June 24, 2002 has been received with all cited references and made of record. See individual IDS's for references not made of record for lack of complete bibliographic information.

Claims **1-107** remain in the case.

The disclosure is objected to because of the following informalities:

Incorporation by reference of essential material by reference to a foreign application or a foreign patent or to a publication inserted in the specification is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by applicant, or a practitioner representing applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCAP 1973); *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

In each of the above cases, the incorporations are of the complete document, and fails to properly point out the particular portions of the US patent(s) being incorporated; see MPEP §608.01(p)(1)(A) noting *In re de Seversky* and in the same paragraph (column 2 of p. 600-769, August 2001 edition) the instruction which reads as follows: "[p]articular attention should be directed to specific portions of the referenced document wherein the subject matter being incorporated may be found."

In addition, each of the above incorporations represents a failure to provide specific disclosure of how to make and/or use. Therefore, the above citations of the *Hawkins* decisions continue to apply to all incorporations by reference.

The attempt to incorporate subject matter into this application by reference to patents and to non-patent literature at pages 110, lines 22 and 25-26, and page 111, lines 8-9 of the disclosure is improper because the incorporated has not been made as required by the *Hawkins* and related decisions noted above.

Chemical name provided in the Example at page 83 appears to be incorrect:

i) at page 83 at line 3, the term "quinolin-3-one" appears to include a type; did applicant intend the term to read -- quinolin-8-one --?

Appropriate correction is required.

Claims **1-55 and 58-107** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention; the scope is excessive in view of the disclosed exemplifications.

The definitions of substituents in claim **1** is directed to a vast number of chemical compounds which have not been described in the instant disclosure in a manner permitting the ordinary practitioner to have the guidance necessary to make a very large proportion of the compounds encompassed. Examiner finds only about 150 compounds which are precursors, intermediates or final products (variously substituted [1,4]oxazino[2,3-*f*]quinolin-8-ones) provided in the "Examples" section. No other tricyclic ring nucleus has been disclosed as having been synthesized within the examples. And additionally none of the exemplary compounds discloses a structure with the multiple layers of substituents on top of substituents provided for by the noted claim or provides a complete description of how to make same.

Applicant is respectfully requested to substantially narrow the scope of the instant generic and sub-generic claims to reflect the scope of the contribution actually made.

And lastly, claims **78 and 79** directed to determining the presence of an andogen receptor, and to purification of an androgen receptor containing sample, respectively, are entirely beyond the scope of any practical teaching of any exemplification of the instant disclosure and therefore the cancellation of same is respectfully requested.

Claims **1-55 and 58-107** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the compound claims is excessive because of the presence of numerous Markush groups and nested Markush groups; see claim **1** in particular. In addition, the repeated use of the term "may be optionally substituted" without specifying the substituents implied thereby renders the breadth excessive because said term implies that the unnamed substituents is/are open to all possible alternatives. In method of treatment claims **80-107**, the breadth of the claims is also excessive because of the presence claim **80** of the term "having a condition mediated by an androgen receptor," which extends to all such conditions, known and unknown, and without specific test data to substantiate any one disease treatment. Additionally, the terms "a [disease] process mediated by an anabolic agent" and "cancer" appearing in claims **93 and 107** are both excessively broad in view of their generic coverage of areas which are not properly referred to generically when treatments are proposed in the absence of adequate supporting evidence.

B. The nature of the invention includes a method of testing, a method of purification, and a vast number of methods of medicinal treatment wherein compounds of instant claim **1** are administered to a host in need of said treatment. Claims **1-55 and 58-76** are directed to a vast array of compounds defined by a series of Markush groups and pharmaceutical compositions thereof.

C. The state of the prior art is defined by the prior art presently cited by applicant and by examiner and particularly by PTO-892 references **F and G** wherein anticipatory compounds and compositions have been disclosed.

D. The level of one of ordinary skill in the relevant chemical synthesis arts is high because the syntheses of many compounds very closely analogous to the instant claimed

compounds are known in the art (PTO-892 references **F and G**). However, the level of one of ordinary skill in the medical arts is moderate because it is unclear which if any of the compounds disclosed herein are active against one or more specific disease conditions.

E. The level of predictability in the art is indeterminate in light of the instant disclosure wherein there is no clear showing that compounds which are active as androgen receptor agonists or antagonists are actually effective in the treatment of any specific disease condition. If applicant has additional art bearing on this question, examiner respectfully requests submission of same as applicant's earliest convenience.

F. The amount of direction provided by the inventor is limited to the chemical syntheses of numerous [1,4]oxazino[2,3-*f*]quinolin-8-ones and data identifying which compounds are antagonists and which are agonists in the presence of known androgen receptors. However, no other chemical species have been disclosed as having been synthesized, isolated, or subjected to any test regimen to determine possible medicinal activity. Also, no data or other guidance has been provided to support claims directed to the treatment of one or more of the numerous specific disease conditions listed in claims **85, 86, 90, 91, 93-94, 100-101 and 107**.

G. The existence of working examples is limited to those noted in the previous section of this rejection.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because the instant specification only discloses how to make compounds with a [1,4]oxazino[2.3-*f*]isoquinolin-8-one ring system, the 8-O-protected analogues, thereof and precursors prepared during the synthesis thereof. In addition the specification only discloses biological testing results limited i) to testing of the compounds noted, and ii) wherein the testing is limited to showings of agonist or antagonist activity in the presence of a receptor, but no showing of efficacy in the treatment of any one of the specific disease conditions listed in any of claims **85, 86, 90, 91, 93-94, 100-101 and 107**. Applicant is respectfully requested to provide additional data to support specific methods of treatment claims or to delete claims **80-107** directed to same. While applicant has shown that the compounds disclosed herein have potential utility in the treatment of disease conditions wherein an androgen-sensitive receptor has been implicated, there has been no showing that any particular disease condition may be effectively treated by administration of any single

compound of claim **1** to any host, including cells in culture. Applicant is further reminded that claims directed to the treatment of "cancer" and "HIV" still require an evidentiary showing in support of same: e.g. see MPEP §2107.03 (III) and therein *Ex parte Balzarini,* 21 USPQ 2d 1892 (Bd Pat App & Inter, 1992) and other cases for guidance concerning enablement for medicinal claims. And lastly, claims **78 and 79** are not enabled by any specific embodiments and therefore would clearly require undue experimentation in view of the complete absence of guidance in the form of an example directed to how to practice the subject matter of either claim.

Claim **101** is objected to because of the following informalities:

The second claim numbered "**101**" is improperly numbered and has been renumbered as claim -- **102** -- under the authority of
37 C.F.R. §1.126. Applicant is respectfully requested to make this change in all subsequent submissions.

Appropriate correction is required.

Claims **1-7, 9, 11-18, 20-21, 23-36, 39, 41, 45, 49-51, 56-58, 60-74, 76-77 and 86-107** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims **1** (lines 14, 19, 24, 37, 48, 52, 56, 59, 63, 66, 70, 73, 76, 80, 84-88 and 90), **2-7, 9, 11-18, 20-21, 23-36, 39, 41, 45, 49** (many), **50** (many), **51, 56-57, 58** (many), **60-74, 76-77, 85-86, 89-90, 93-94 and 101-102**, the term "selected from the group of" is incomplete because Markush groups are properly formulated with the term -- selected from the group **consisting** of [A], [B], ... and [R] --. See MPEP §2173.05(h)(I). See also claim **57** at line 26 wherein the Markush group format is incomplete because the term -- and -- is missing.

In claims **1** (lines 17-18, 23, 28, 40-41, 50-51, 54-55, 58, 61-62, 65, 69, 72, 74-75, 78-79, 83), **2** (lines 3-4), **3, 5-7, 9, 11-18, 20-21, 23, 25, 27, 29-30, 32, 35, 49** (lines 4, 8, 11, 16, 20), **50** (lines 3-4, 6-7, 12, 17), **58** (lines 7-8, 13, 18, 30-31, 40-41, 44-45, 48, 51-52, 55, 59, 62, 64-65, 68-69, 73), **60-62, 64-71 and 73-74** the term "may be optionally substituted" is incomplete

for failure to specify the substituents implied thereby. See also claims **4, 22, 24, 28 and 36** wherein the term "optionally substituted" has the same problem.

Claim **61** is incomplete because the term
-- comprising a compound -- is missing following the term "composition" at line 1.

In claim **87** the term "modulate" found is indefinite for failure to indicate what specific treatment action(s) or effect(s) is(are) intended by said term and which particular compound(s) is(are) associated with each specific effect(s). The same problem extends to dependent claims **88-107**.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

(e) the invention was described in

(1) an application for patent described under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application filed under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)."

Claims **1-7, 9, 11, 12-14, 16-22, 27-28, 37, 41-42, 53, 58-62, 64, 66-68, 73, 75, 80, 82 and 85-107** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Marui et al. '967** (PTO-892 ref. **F**).

Applicant is referred to the following compounds each of which read on the instant noted claims: structures XIV & XV (col. 46); structures XVIII, XIX, XXI and XXII (cols. 47-48); compound named at col. 64, lines 21-24; compound pictured at col. 68 at line 35. See also the abstract of the noted references wherein medicinal treatments are also taught.

Claims **1-7, 9, 11, 12-14, 16-22, 27-28, 37, 41-42, 53, 58-62, 64, 66-68, 73, 75, 80, 82 and 85-107** are rejected under 35 U.S.C. §102(e) as being anticipated by **Marui et al. '704** (PTO-892 ref. **G**).

Applicant is requested to note the following compounds which read on the instant claims: the compound named at column 38, lines 20-21; the compound disclosed at column 44, lines 24-35; the compound disclosed at column 50 at lines 44-55; the compound disclosed at column 51, lines 1-25; the compound disclosed at column 52, lines 45-55; the compounds disclosed at column 53 at lines 5-15, 28-40 and 49-60; the compounds disclosed at column 54 at lines 6-15 and 26-35; the compound disclosed at column 61 at lines 4-15; the compound disclosed at column 69 at lines 7-20 and 50-60; the compound disclosed at column 72 at lines 5-15; the compound disclosed at column 74 at lines 43-55; the compound disclosed at column 75 at lines 3-15; the four compound disclosed at columns 77-78 at lines 4-20 and 39-50; the four compound disclosed at columns 79-80; the four compounds disclosed at columns 81-82; the compounds disclosed at column 83 at lines 4-20 and 40-55; and the subject matter disclosed in claims ***1, 14 and 15***.

Claims **8, 10, 15, 23-26, 29-36, 38-40, 43-52, 54-57, 63, 65, 69-72, 74, 76-79, 81 and 83-84** would be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. §112.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(f) or (g) prior art under 35 U.S.C. §103(a).

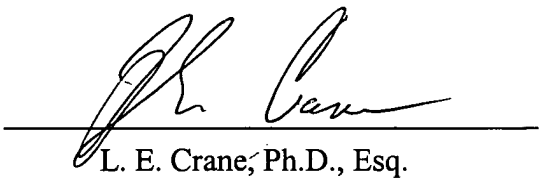
Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 703-872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at **571-272-0661**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
07/19/2004



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